



## xeroderma pigmentosum

Xeroderma pigmentosum, which is commonly known as XP, is an inherited condition characterized by an extreme sensitivity to ultraviolet (UV) rays from sunlight. This condition mostly affects the eyes and areas of skin exposed to the sun. Some affected individuals also have problems involving the nervous system.

The signs of xeroderma pigmentosum usually appear in infancy or early childhood. Many affected children develop a severe sunburn after spending just a few minutes in the sun. The sunburn causes redness and blistering that can last for weeks. Other affected children do not get sunburned with minimal sun exposure, but instead tan normally. By age 2, almost all children with xeroderma pigmentosum develop freckling of the skin in sun-exposed areas (such as the face, arms, and lips); this type of freckling rarely occurs in young children without the disorder. In affected individuals, exposure to sunlight often causes dry skin (xeroderma) and changes in skin coloring (pigmentation). This combination of features gives the condition its name, xeroderma pigmentosum.

People with xeroderma pigmentosum have a greatly increased risk of developing skin cancer. Without sun protection, about half of children with this condition develop their first skin cancer by age 10. Most people with xeroderma pigmentosum develop multiple skin cancers during their lifetime. These cancers occur most often on the face, lips, and eyelids. Cancer can also develop on the scalp, in the eyes, and on the tip of the tongue. Studies suggest that people with xeroderma pigmentosum may also have an increased risk of other types of cancer, including brain tumors. Additionally, affected individuals who smoke cigarettes have a significantly increased risk of lung cancer.

The eyes of people with xeroderma pigmentosum may be painfully sensitive to UV rays from the sun. If the eyes are not protected from the sun, they may become bloodshot and irritated, and the clear front covering of the eyes (the cornea) may become cloudy. In some people, the eyelashes fall out and the eyelids may be thin and turn abnormally inward or outward. In addition to an increased risk of eye cancer, xeroderma pigmentosum is associated with noncancerous growths on the eye. Many of these eye abnormalities can impair vision.

About 30 percent of people with xeroderma pigmentosum develop progressive neurological abnormalities in addition to problems involving the skin and eyes. These abnormalities can include hearing loss, poor coordination, difficulty walking, movement problems, loss of intellectual function, difficulty swallowing and talking, and seizures. When these neurological problems occur, they tend to worsen with time.

Researchers have identified at least eight inherited forms of xeroderma pigmentosum: complementation group A (XP-A) through complementation group G (XP-G) plus a

variant type (XP-V). The types are distinguished by their genetic cause. All of the types increase skin cancer risk, although some are more likely than others to be associated with neurological abnormalities.

## Frequency

Xeroderma pigmentosum is a rare disorder; it is estimated to affect about 1 in 1 million people in the United States and Europe. The condition is more common in Japan, North Africa, and the Middle East.

## Genetic Changes

Xeroderma pigmentosum is caused by mutations in genes that are involved in repairing damaged DNA. DNA can be damaged by UV rays from the sun and by toxic chemicals such as those found in cigarette smoke. Normal cells are usually able to fix DNA damage before it causes problems. However, in people with xeroderma pigmentosum, DNA damage is not repaired normally. As more abnormalities form in DNA, cells malfunction and eventually become cancerous or die.

Many of the genes related to xeroderma pigmentosum are part of a DNA-repair process known as nucleotide excision repair (NER). The proteins produced from these genes play a variety of roles in this process. They recognize DNA damage, unwind regions of DNA where the damage has occurred, snip out (excise) the abnormal sections, and replace the damaged areas with the correct DNA. Inherited abnormalities in the NER-related genes prevent cells from carrying out one or more of these steps. The *POLH* gene also plays a role in protecting cells from UV-induced DNA damage, although it is not involved in NER; mutations in this gene cause the variant type of xeroderma pigmentosum.

The major features of xeroderma pigmentosum result from a buildup of unrepaired DNA damage. When UV rays damage genes that control cell growth and division, cells can either die or grow too fast and in an uncontrolled way. Unregulated cell growth can lead to the development of cancerous tumors. Neurological abnormalities are also thought to result from an accumulation of DNA damage, although the brain is not exposed to UV rays. Researchers suspect that other factors damage DNA in nerve cells. It is unclear why some people with xeroderma pigmentosum develop neurological abnormalities and others do not.

Inherited mutations in at least eight genes have been found to cause xeroderma pigmentosum. More than half of all cases in the United States result from mutations in the *XPC*, *ERCC2*, or *POLH* genes. Mutations in the other genes generally account for a smaller percentage of cases.

## Inheritance Pattern

This condition is inherited in an autosomal recessive pattern, which means both copies of the gene in each cell have mutations. The parents of an individual with an autosomal

recessive condition each carry one copy of the mutated gene, but they typically do not show signs and symptoms of the condition.

### **Other Names for This Condition**

- DeSanctis-Cacchione syndrome
- XP

### **Diagnosis & Management**

These resources address the diagnosis or management of xeroderma pigmentosum:

- American Cancer Society: How are Squamous and Basal Cell Skin Cancer Diagnosed?  
<http://www.cancer.org/cancer/basal-and-squamous-cell-skin-cancer/detection-diagnosis-staging/how-diagnosed.html>
- American Cancer Society: How is Melanoma Diagnosed?  
<http://www.cancer.org/cancer/melanoma-skin-cancer/detection-diagnosis-staging/how-diagnosed.html>
- GeneReview: Xeroderma Pigmentosum  
<https://www.ncbi.nlm.nih.gov/books/NBK1397>
- Genetic Testing Registry: Xeroderma pigmentosum  
<https://www.ncbi.nlm.nih.gov/gtr/conditions/C0043346/>
- Genetic Testing Registry: Xeroderma pigmentosum, complementation group b  
<https://www.ncbi.nlm.nih.gov/gtr/conditions/C1970808/>
- Genetic Testing Registry: Xeroderma pigmentosum, group C  
<https://www.ncbi.nlm.nih.gov/gtr/conditions/C2752147/>
- Genetic Testing Registry: Xeroderma pigmentosum, group D  
<https://www.ncbi.nlm.nih.gov/gtr/conditions/C0268138/>
- Genetic Testing Registry: Xeroderma pigmentosum, group E  
<https://www.ncbi.nlm.nih.gov/gtr/conditions/C1848411/>
- Genetic Testing Registry: Xeroderma pigmentosum, group F  
<https://www.ncbi.nlm.nih.gov/gtr/conditions/C0268140/>
- Genetic Testing Registry: Xeroderma pigmentosum, group G  
<https://www.ncbi.nlm.nih.gov/gtr/conditions/C0268141/>
- Genetic Testing Registry: Xeroderma pigmentosum, type 1  
<https://www.ncbi.nlm.nih.gov/gtr/conditions/C0268135/>
- Genetic Testing Registry: Xeroderma pigmentosum, variant type  
<https://www.ncbi.nlm.nih.gov/gtr/conditions/C1848410/>

- MedlinePlus Encyclopedia: Xeroderma Pigmentosum  
<https://medlineplus.gov/ency/article/001467.htm>
- National Cancer Institute: Melanoma Treatment  
<https://www.cancer.gov/types/skin/patient/melanoma-treatment-pdq>
- National Cancer Institute: Skin Cancer Treatment  
<https://www.cancer.gov/types/skin/patient/skin-treatment-pdq>
- Xeroderma Pigmentosum Society, Inc.: Beta Carotene  
<https://www.xps.org/single-post/2015/04/08/To-Beta-Carotene-or-Not-To-Beta-Carotene>
- Xeroderma Pigmentosum Society, Inc.: Ultraviolet Radiation and Protection  
<https://www.xps.org/single-post/2015/04/08/Ultraviolet-Radiation-Protection>

These resources from MedlinePlus offer information about the diagnosis and management of various health conditions:

- Diagnostic Tests  
<https://medlineplus.gov/diagnostictests.html>
- Drug Therapy  
<https://medlineplus.gov/drugtherapy.html>
- Surgery and Rehabilitation  
<https://medlineplus.gov/surgeryandrehabilitation.html>
- Genetic Counseling  
<https://medlineplus.gov/geneticcounseling.html>
- Palliative Care  
<https://medlineplus.gov/palliativecare.html>

## **Additional Information & Resources**

### MedlinePlus

- Encyclopedia: Xeroderma Pigmentosum  
<https://medlineplus.gov/ency/article/001467.htm>
- Health Topic: Skin Cancer  
<https://medlineplus.gov/skincancer.html>
- Health Topic: Skin Pigmentation Disorders  
<https://medlineplus.gov/skinpigmentationdisorders.html>

### Genetic and Rare Diseases Information Center

- Xeroderma pigmentosum  
<https://rarediseases.info.nih.gov/diseases/7910/xeroderma-pigmentosum>

### Additional NIH Resources

- National Cancer Institute: Melanoma  
<https://www.cancer.gov/types/eye>
- National Cancer Institute: Skin Cancer  
<https://www.cancer.gov/types/skin>
- National Institutes of Health Clinical Center: Understanding Xeroderma Pigmentosum  
[https://www.cc.nih.gov/ccc/patient\\_education/pepubs/xp7\\_17.pdf](https://www.cc.nih.gov/ccc/patient_education/pepubs/xp7_17.pdf)

### Educational Resources

- Disease InfoSearch: Xeroderma pigmentosum  
<http://www.diseaseinfosearch.org/Xeroderma+pigmentosum/7564>
- MalaCards: ercc2-related xeroderma pigmentosum  
[http://www.malacards.org/card/ercc2\\_related\\_xeroderma\\_pigmentosum](http://www.malacards.org/card/ercc2_related_xeroderma_pigmentosum)
- MalaCards: polh-related xeroderma pigmentosum  
[http://www.malacards.org/card/polh\\_related\\_xeroderma\\_pigmentosum](http://www.malacards.org/card/polh_related_xeroderma_pigmentosum)
- MalaCards: xpc-related xeroderma pigmentosum  
[http://www.malacards.org/card/xpc\\_related\\_xeroderma\\_pigmentosum](http://www.malacards.org/card/xpc_related_xeroderma_pigmentosum)
- Orphanet: Xeroderma pigmentosum  
[http://www.orpha.net/consor/cgi-bin/OC\\_Exp.php?Lng=EN&Expert=910](http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=910)
- Prevent Blindness America: Protect Your Eyes from the Sun  
<http://www.preventblindness.org/protect-your-eyes-sun>

### Patient Support and Advocacy Resources

- National Organization for Rare Disorders (NORD)  
<https://rarediseases.org/rare-diseases/xeroderma-pigmentosum/>
- Resource list from the University of Kansas Medical Center  
<http://www.kumc.edu/gec/support/xeroderm.html>
- Skin Cancer Foundation  
<http://www.skincancer.org/>
- Xeroderma Pigmentosum Society, Inc.  
<http://www.xps.org/>
- XP Family Support Group  
<http://www.xpfamilysupport.org/>

### GeneReviews

- Xeroderma Pigmentosum  
<https://www.ncbi.nlm.nih.gov/books/NBK1397>

### Genetic Testing Registry

- Xeroderma pigmentosum  
<https://www.ncbi.nlm.nih.gov/gtr/conditions/C0043346/>
- Xeroderma pigmentosum, complementation group b  
<https://www.ncbi.nlm.nih.gov/gtr/conditions/C1970808/>
- Xeroderma pigmentosum, group C  
<https://www.ncbi.nlm.nih.gov/gtr/conditions/C2752147/>
- Xeroderma pigmentosum, group D  
<https://www.ncbi.nlm.nih.gov/gtr/conditions/C0268138/>
- Xeroderma pigmentosum, group E  
<https://www.ncbi.nlm.nih.gov/gtr/conditions/C1848411/>
- Xeroderma pigmentosum, group F  
<https://www.ncbi.nlm.nih.gov/gtr/conditions/C0268140/>
- Xeroderma pigmentosum, group G  
<https://www.ncbi.nlm.nih.gov/gtr/conditions/C0268141/>
- Xeroderma pigmentosum, type 1  
<https://www.ncbi.nlm.nih.gov/gtr/conditions/C0268135/>
- Xeroderma pigmentosum, variant type  
<https://www.ncbi.nlm.nih.gov/gtr/conditions/C1848410/>

### ClinicalTrials.gov

- ClinicalTrials.gov  
<https://clinicaltrials.gov/ct2/results?cond=%22xeroderma+pigmentosum%22>

### Scientific articles on PubMed

- PubMed  
<https://www.ncbi.nlm.nih.gov/pubmed?term=%28Xeroderma+Pigmentosum%5BM%5D%29+AND+%28xeroderma+pigmentosum%5BTIAB%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1800+days%22%5Bdp%5D>

## OMIM

- XERODERMA PIGMENTOSUM, COMPLEMENTATION GROUP A  
<http://omim.org/entry/278700>
- XERODERMA PIGMENTOSUM, COMPLEMENTATION GROUP B  
<http://omim.org/entry/610651>
- XERODERMA PIGMENTOSUM, COMPLEMENTATION GROUP C  
<http://omim.org/entry/278720>
- XERODERMA PIGMENTOSUM, COMPLEMENTATION GROUP D  
<http://omim.org/entry/278730>
- XERODERMA PIGMENTOSUM, COMPLEMENTATION GROUP E  
<http://omim.org/entry/278740>
- XERODERMA PIGMENTOSUM, COMPLEMENTATION GROUP F  
<http://omim.org/entry/278760>
- XERODERMA PIGMENTOSUM, COMPLEMENTATION GROUP G  
<http://omim.org/entry/278780>
- XERODERMA PIGMENTOSUM, VARIANT TYPE  
<http://omim.org/entry/278750>

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*Free article on PubMed Central:* <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2288663/>
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